

CLINICAL RESEARCH

## **Efficacy of modified Duhuo Jisheng decoction combined with diosmine in the treatment of lumbar spinal stenosis and its effect on serum factors**

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### **Keywords**

Duhuo Jisheng decoction, Diosmin;  
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### **Abstract**

**Objective** To analyze the efficacy of modified Duhuo Jisheng decoction combined with diosmine in the treatment of lumbar spinal stenosis (LSS) and its effect on serum factors. **Methods** 118 patients with LSS who were treated in our hospital from February 2019 to February 2022 were randomly divided into a control group and an observation group, with 59 cases in each group. Patients in both groups were given conventional treatment, and patients in the control group was given diosmine on this basis, while patients in the observation group was given a modified Duhuo Jisheng decoction treatment on the basis of the control group. The traditional Chinese medicine (TCM) symptom scores, serum factor level and scores of visual analog scale (VAS), Oswestry Disability Index questionnaire (ODI), and activity of daily living (ADL) scores were compared between the two groups. **Results** After treatment, in both groups, 6 items of TCM symptom scores, neuropeptide Y (NPY), 5-hydroxytryptamine (5-HT), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-6 (IL-6) levels and scores of VAS and ODI were significantly lower than those before treatment ( $P<0.05$ ), and these levels in the observation group were significantly lower than those in the control group ( $P<0.05$ ); after treatment, the ADL score of the two groups was significantly higher than that before treatment ( $P<0.05$ ), and the ADL score of the observation group was significantly higher than that of the control group ( $P<0.05$ ). **Conclusion** The combination of modified Duhuo Jisheng decoction and diosmin can effectively alleviate the clinical symptoms of patients with LSS, help to regulate serum factor levels, reduce the pain of patients, and improve the ability of daily living and the activities of patients.

## Introduction

Lumbar spinal stenosis (LSS) refers to the clinical syndrome caused by the reduction of the volume of spinal canal, nerve canal or intervertebral foramen due to osseous or fibrous hyperplasia and intervertebral disc herniation, which compresses the cauda equina nerve and nerve root in the spinal canal to cause ischemia and edema [1]. LSS patients are mainly characterized by low back and leg pain and intermittent claudication. In severe cases, they may have symptoms of defecation and sexual life disorder. At present, the clinical treatment methods of LSS patients include surgery, minimally invasive surgery or treatment, conservative treatment, etc. When there is no obvious surgical indication, most patients prefer drug conservative treatment [2]. Diosmin is a vascular protective agent, which can inhibit edema and improve local microcirculation. It has a good effect on LSS in the short term, but its long-term effect is not ideal, and adverse reactions, such as gastrointestinal reaction and headache, may occur after long-term use. Therefore, the clinical use of diosmin is limited. Studies have shown that integrated traditional Chinese and Western medicine has good long-term curative effect and few adverse effects in the treatment of LSS, and it is easily accepted by patients [3]. Traditional Chinese medicine (TCM) has ascribed LSS to the category of "Bi Zheng" (arthralgia syndrome) and "Yao Tong" (low back pain), which is caused by invade of cold dampness and stagnation of Qi and blood. Duhuo Jisheng decoction is a classic formula for dispelling wind and eliminating dampness derived from the well-known medical scientist in the Tang Dynasty Simiao Sun's "Beiji Qianjin Yaofang" (Prescriptions Worth a Thousand Pieces of Gold for Emergencies), and is commonly used in clinic to treat patients with wind-cold-dampness type of arthralgia and deficiency of the vital-Qi, which focuses on the pathogenesis of LSS [4]. The purpose of this study is to explore the clinical effect of modified Duhuo Jisheng decoction combined with diosmin in the treatment of patients with LSS and its effect on serum factors so as to provide reference for clinical treatment, and the results of this study are reported below.

## Materials and methods

### General data

A total of 118 patients with LSS who were diagnosed in our hospital from February 2019 to February 2022 were selected as the study subjects and randomly divided into observation and control groups. The control group consisted of 59 patients, 30 males and 29 females. The pathological features of the patient are as follows: age: 41 to 74 ( $56.4 \pm 6.85$ ) years; disease duration: 1.8-6.81 ( $4.68 \pm 1$ ) years; lesion location: 28 cases at L<sub>3-4</sub> segment, 18 cases at L<sub>4-5</sub> segment and 13 cases at L<sub>5-S1</sub> segment. The observation group consisted of 59 patients, 34 males and 25 females, whose pathological features were as follows: age: 42 to 68 ( $55.1 \pm 6.89$ ) years; disease duration: 2.73-6.96 ( $4.82 \pm 0.93$ ) years; lesion location: 25 cases at L<sub>3-4</sub> segment, 16 cases at L<sub>4-5</sub> segment and 18 cases at L<sub>5-S1</sub> segment. There were no significant differences in baseline data such as gender, age, disease duration, and lesion location between the two groups ( $P > 0.05$ ), and this study was approved by the medical ethics committee, with the patients' informed consent.

### Inclusion criteria

(1) Those who meet the typical clinical symptoms of LSS with deficiency of kidney Qi in the *Guidelines for diagnosis and treatment of common orthopaedic diseases of traditional Chinese medicine* [5]. The main symptoms are waist and leg pain, mental fatigue, muscle wasting, and the secondary symptoms are shortness of breath and spontaneous sweating, fatigue, weakness, and pale complexion. (2) The diagnosis of LSS is confirmed by imaging studies including computed tomography (CT), magnetic resonance imaging (MRI), and laminography. (3) Those whose clinical data are complete and do not meet the surgical indications.

### Exclusion criteria

(1) Those with history of relevant drug allergies; (2) Those with malignant tumor, cognitive dysfunction, mental disorder and abnormal immune function; (3) Those combined with liver, kidney, heart, lung and

other important organ dysfunction.

### Treatment

Patients in both groups were given conventional treatments of Western medicine such as pain relief and rehabilitation training. And patients in the control group was given diosmin tablets (Nanjing Zhengda Tianqing Pharmaceutical Co., Ltd., approve number of NMPA: H20058471, specification: 0.45 g\*20 tablets), 1 tablet/time for 2 times/day (d). The observation group was treated with modified Duhuo Jisheng decoction based on the control group, which consisted of: 15 g each of Duhuo (*Heracleum hemsleyanum* Diels), Fangfeng (*Saposhnikovia divaricata* Schischk), Qinjiao (*Gentiana macrophylla*), Danggui (*Angelica sinensis*) and Dangsheng (*Codonopsis pilosula* Nannf), 10 g each of Duzhong (*Eucommia ulmoides* Oliver), Sangjisheng (*Taxillus sutchuenensis* Danser), Chuanniuxi (*Cyathula officinalis* Kuan), Xixin (*Asarum sieboldii* Miq.), Chuanxiong (*Ligusticum chuanxiong hort*) and Guizhi (*Cinnamomum cassia* Presl), 3 g of Xixin, and 6 g of Gancào (*Glycyrrhiza uralensis* Fisch.). The addition and subtraction of the prescription was performed with the syndrome: 8 g of Suoyang (*Songaria cynomorium* herb) for patients with Yang deficiency; 10 g of Sharen (*Amomum villosum* Lour.) and Baizhu (*Atractylodes macrocephala* Koidz.) for patients with spleen deficiency; 10 g of Cangzhu (*Atractylodes chinensis* Koidz.) and Yanhusuo (*Corydalis yanhusuo*) for patients with pain. The treatment lasted for 8 weeks.

### Detection indexes

(1) TCM symptom scores [6]: before treatment and 8 weeks after treatment, patients in both groups were scored according to the clinical severity of symptoms. Primary symptoms: waist and leg pain, mental fatigue, and muscle wasting, with a score range from 0 to 6 points. Secondary symptoms: shortness of breath and spontaneous sweating, fatigue and weakness, pale complexion, with a score range of 0 to 3 points, with higher scores representing more severe symptoms; (2) Serum factors: 5 ml of fasting venous blood was

collected in the early morning from patients in the two groups before and 8 weeks after treatment, and enzyme-linked immunosorbent assay (ELISA) was used to detect neuropeptide Y (NPY), 5-hydroxytryptamine (5-HT), TNF- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 (IL-6) levels, and ELISA kits were purchased from Beijing Yiqiao Shenzhou Technology Co., Ltd. (3) Visual analog scale (VAS) [3], Oswestry Disability Index questionnaire (ODI) [2], activities of daily living (ADL) [7] scores: VAS was used to assess the pain levels of patients in both groups before and after 8 weeks of treatment, with higher VAS scores representing higher levels of pain. Lumbar joint mobility function of patients in both groups was assessed using ODI, and higher ODI scores indicated more restricted lumbar mobility function; ADL was used to evaluate the activities of daily living of patients, and a higher ADL score suggested a stronger ability to perform activities of daily living.

### Statistical analysis

Statistical analysis was performed using GraphPad 8.0. Paired samples t-test was applied for comparison with the data before treatment in the same group; Independent samples t-test was applied for comparison with the data in the control group during the same period of treatment.  $P < 0.05$  was taken as statistically significant.

### Results

#### Comparison of TCM symptom scores between the two groups

After treatment, the scores of 6 items of TCM symptoms (waist and leg pain, mental fatigue, muscle wasting, shortness of breath and spontaneous sweating, fatigue and weakness, pale complexion) of patients in the two groups were significantly lower than those before treatment ( $P < 0.05$ ), and the scores in the observation group were remarkably lower than those in the control group ( $p < 0.05$ ), as shown in Table 1.

#### Comparison of serum factor levels before and after treatment between the two groups

After treatment, the levels of NPY, 5-HT, TNF- $\alpha$  and IL-6 of patients in the two groups were observably

lower than those before treatment ( $P<0.05$ ), and the levels in the observation group were evidently lower than those in the control group ( $P<0.05$ ), as shown in Table 2.

#### Comparison of VAS, ODI and ADL scores before and after treatment between the two groups

After treatment, the scores of VAS and ODI of patients in the two groups were largely lower than

those before treatment ( $P<0.05$ ), and the scores in the observation group were significantly lower than those in the control group ( $P<0.05$ ). After treatment, the ADL score of the two groups was obviously higher than that before treatment ( $P<0.05$ ), and the ADL score of the observation group was significantly higher than that of the control group ( $P<0.05$ ), as displayed in Table 3.

Table 1 Comparison of TCM symptom scores before and after treatment between two groups of patients with LSS ( $\bar{x}\pm s$ , points)

Group	Time	Waist and leg pain	Mental fatigue	Muscle wasting	Shortness of breath and spontaneous sweating	Fatigue and weakness	Pale complexion
Control group	Before treatment	3.75±0.62	3.15±0.75	3.11±0.65	1.70±0.45	1.55±0.35	1.54±0.35
	After treatment	2.62±0.43*	2.41±0.47*	1.92±0.45*	1.35±0.36*	1.25±0.3*	1.07±0.27*
Observation group	Before treatment	3.87±0.60	3.25±0.70	3.15±0.62	1.75±0.35	1.65±0.31	1.56±0.35
	After treatment	2.12±0.39* <sup>^</sup>	1.93±0.44* <sup>^</sup>	1.65±0.30* <sup>^</sup>	1.08±0.25* <sup>^</sup>	1.06±0.23* <sup>^</sup>	0.85±0.26* <sup>^</sup>

Note: Compared with the same group before treatment: \* $P<0.05$ ; Compared with the control group at the same period of treatment: <sup>^</sup> $P<0.05$ .

Table 2 Comparison of serum factor levels between the two groups ( $\bar{x}\pm s$ )

Group	Time	NPY (pg/L)	5-HT (IU/L)	TNF- $\alpha$ ( $\mu$ g/L)	IL-6 ( $\mu$ g/L)
Control group	Before treatment	187.52±26.20	1510.63±325.18	1.95±0.47	133.68±22.12
	After treatment	157.94±23.72*	1176.59±336.45*	1.51±0.39*	99.37±17.70*
Observation group	Before treatment	188.11±25.32	1526.75±328.45	1.92±0.45	137.25±22.12
	After treatment	136.54±20.30* <sup>^</sup>	960.15±203.25* <sup>^</sup>	1.10±0.31* <sup>^</sup>	86.55±16.05* <sup>^</sup>

Note: Compared with the same group before treatment: \* $P<0.05$ ; Compared with the control group at the same period of treatment: <sup>^</sup> $P<0.05$ .

Table 3 Comparison of VAS, ODI and ADL scores before and after treatment between the two groups ( $\bar{x}\pm s$ )

Group	Time	VAS/points	ODI/points	ADL/points
Control group	Before treatment	5.85±1.12	31.12±5.15	45.85±5.45
	After treatment	1.29±0.39*	12.78±3.37*	66.36±8.74*
Observation group	Before treatment	5.92±1.15	30.15±5.25	45.98±5.35
	After treatment	0.75±0.36 <sup>^</sup>	8.45±2.58 <sup>^</sup>	73.15±8.96 <sup>^</sup>

Note: Compared with the same group before treatment: \* $P<0.05$ ; Compared with the control group at the same period of treatment: <sup>^</sup> $P<0.05$ .

### Discussion

LSS is a common disease of low back and leg pain. Its pathogenic factors include primary spinal canal stenosis and secondary factors (eg. hypertrophy of ligamentum flavum, small joints, and vertebral lamina), and its main characteristics are persistent low back and leg pain and intermittent claudication [8]. The mainstays of Western medicine for the treatment of LSS include surgical procedures, medical therapy, rehabilitation training, etc. Based on the fact that LSS mostly occurs in the middle-aged and elderly population, most patients are combined with different degrees of osteoporosis or hyperlipidemia, coronary heart disease, and other basic diseases, making postoperative complications common. Therefore, many patients usually choose drug conservative treatment. Diosmine is one of the common drugs used in the clinical treatment of LSS in Western medicine. Although its short-term efficacy is good, there are still many disadvantages in long-term administration with many adverse reactions. In the theory of TCM, LSS belongs to the category of "Bi Zheng", "Yao Tong" and "Wei Zheng" (flaccid syndrome), and it is divided into three syndrome types: wind-cold obstruction, Qi deficiency and blood stasis, and liver and kidney deficiency. As recorded in the "Jin Kui Yi" (The Wings of the Golden Coffer): "Congestion and low back pain appeared.....sluggishness of blood circulation, and stagnation of meridians". In addition,

it has been pointed out in "Huang Di Nei Jing (Inner Canon of the Yellow Emperor)-Su Wen-Bi lun" that "wind, cold and dampness combine to form arthralgia". This disease is a syndrome of deficiency in origin and excess in external symptoms, which is based on deficiency of Qi in the kidney and liver, obstruction of meridians and collaterals, and Qi stagnation and blood stasis. Therefore, it is appropriate to use the prescription of promoting blood circulation and removing blood stasis, nourishing the liver and tonifying the kidney [4]. Duhuo Jisheng decoction can dispel wind and remove dampness, tonify liver and kidney, and conform to the pathogenesis. This study investigated the effect of modified Duhuo Jisheng decoction combined with diosmin on TCM symptoms and serum factors in patients with LSS, and the results showed that the combined treatment had a satisfactory effect.

The results of this study showed that after treatment, the scores of 6 items of TCM symptoms (waist and leg pain, mental fatigue, muscle wasting, shortness of breath and spontaneous sweating, fatigue and weakness, pale complexion) in the two groups were obviously lower than those before treatment, and the scores in the observation group were evidently lower than those in the control group. After treatment, the ADL score of the two groups was markedly higher than that before treatment, and the ADL score of the observation group was remarkably higher than that of

the control group, which suggested that the modified Duhuo Jisheng decoction combined with diosmin can effectively alleviate the clinical symptoms of LSS patients, help to reduce the pain of patients, and improve the ability of daily living and activities of patients. Studies have shown that [9] the occurrence and development of LSS are closely related to venous system obstruction. Firstly, diosmin can improve the effect of norepinephrine, promote the contraction of venous wall and enhance venous tension. Secondly, diosmin can reduce blood concentration, increase blood cell velocity, improve venous microcirculation and reduce obstruction. In the meantime, diosmin can promote lymphatic reflux and alleviate cauda equina nerve or nerve root edema [10]. In the Duhuo Jisheng decoction, Duhuo can dispel wind and relieve pain; Sangjisheng, Duzhong and Niuxi can tonify the liver and kidney; Fangfeng, Xixin, Qinjiao and Guizhi can expel dampness and dissipate cold; Danggui, Shudi, Baishao and Chuanxiong can nourish blood and Yin, replenish essence and nourish kidney; Dangsheng, Fuling and Gancao can replenish Qi. Besides, for those patients with Yang deficiency, it is necessary to add Suoyang to replenish the kidney and strengthen the essence. For those with spleen deficiency, Baizhu was used to invigorate the spleen and replenish Qi, and Sharen was used to warm the spleen and remove dampness. Yanhusuo was added to relieve pain and promote blood circulation in the case of pain, and Cangzhu was added to dispel wind and cold. The whole prescription has the effect of promoting Qi and blood circulation, expelling wind and removing dampness, and tonifying the liver and kidney [11]. Modern pharmacological research shows that Duhuo Jisheng decoction can improve hemorheology, reduce blood viscosity and improve lumbar function. Furthermore, Fangfeng and Qinjiao contain coumarin, lignin and other effective components, which have analgesia and antipyretic effects. The effective components in Duzhong and Niuxi can stimulate vascular endothelial growth factor (VEGF), Wnt and other signaling pathways, and alleviate the symptoms of waist and leg pain [12]. Li Ying et al. [6] have shown that the modified Duhuo Jisheng decoction

combined with diosmin can effectively reduce the degree of spinal canal stenosis and improve the clinical symptoms and lumbar function of LSS patients, which is consistent with the results of this study.

Cauda equina nerve in LSS patients is forced to induce ischemia, edema and tortuosity, which will activate immune system function and release TNF- $\alpha$ , IL-6 and other inflammatory factors, and then aggravate vasospasm to generate low back pain and intermittent lameness. Studies have shown that [13] leukocytes and inflammatory factors are highly expressed in patients with LSS, and their content is positively correlated with the progress of the patient's disease. In addition, inflammation will lead to the increase of 5-HT and NPY levels, both of which are involved in the pain modulation process, and the increase of their levels can cause pain. The results showed that after treatment, the levels of NPY, 5-HT, TNF- $\alpha$  and IL-6 in the observation group were significantly lower than those in the control group, suggesting that modified Duhuo Jisheng decoction combined with diosmin can reduce NPY, 5-HT, TNF- $\alpha$  and IL-6 levels in patients with LSS, and alleviate the body's inflammatory response. Diosmin has the effect of eliminating edema so as to reduce the inflammatory reaction of cauda equina nerve and nerve root. Besides, diosmin can reduce the adhesion between leukocytes and vascular endothelial cells, inhibit the release of inflammatory factors and free radicals, help to reduce the level of oxidative stress and reduce the inflammatory response. Modern pharmacological research shows that [14] Duhuo Jisheng decoction contains coumarins, flavonoids and other effective components, which can inhibit the expression of inflammatory factors such as TNF- $\alpha$ , IL-6 and inducible nitric oxide synthase (iNOS) through multiple channels, and has the efficacy to regulate immunity and reduce inflammation.

In conclusion, the modified Duhuo Jisheng decoction combined with diosmin can effectively alleviate the clinical symptoms of LSS patients, help to regulate the level of serum factors, reduce the pain of patients, and improve the ability of daily living and the

activities of patients.

#### Declaration of conflict-of-interest

The authors declare no conflict-of-interest.

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